ELSEVIER

Burns 29 (2003) 592–595

BURNS

www.elsevier.com/locate/burns

Nutrition and anabolic agents in burned patients

Harald Andel [a,*], Lars-Peter Kamolz [b], Klaus Hörauf [a], Michael Zimpfer [a]

[a] *Department of Anesthesia and Intensive Care, Medical School, University of Vienna 1090, Waehringer Guertel 18-20, Vienna, Austria*
[b] *Division of Plastic and Reconstructive Surgery, Department of Surgery, Medical School, University of Vienna, Vienna, Austria*

Accepted 6 February 2003

Abstract

Purpose of review: Much of the morbidity and mortality of severely burned patients is connected with hypermetabolism and catabolism with its accompanying impairment of wound healing and increased infection risks. In order to prevent the erosion of body mass, nutritional support and other strategies to prevent catabolism have become a major focus in the care of severely burned patients.

Recent findings: Major themes discussed in recent literature are dealing with enteral versus parenteral nutrition and gastric versus duodenal feeding. The possibility of overfeeding is another important aspect of high calorie nutrition as commonly used in burned patients. Specific formulas for enteral nutrition for specific metabolic abnormalities are under evaluation as well as the role of anabolic and anticatabolic agents.

Summary: From the clinical literature, total enteral nutrition starting as early as possible without any supplemental parenteral nutrition is the preferred feeding method for burned patients. Using a duodenal approach, especially in the early postburn phase, seems to be superior to gastric feeding. Administration of high calorie total enteral nutrition in any later septic phase should be critically reviewed due to possible impairment of splanchnic oxygen balance. Therefore, measurement of CO_2-gap should be considered as a monitoring method during small bowel nutrition.

The impact on the course of disease of supplements such as arginine, glutamine and vitamins as well as the impact of the use of anabolic and anticatabolic agents is not yet evident. Furthermore, the effect of insulin administration and low blood sugar regimes on wound healing and outcome in burned patients should be evaluated in future studies.

Keywords: Nutrition; Enteral; Parenteral; Burn; Metabolism

1. Introduction

Catabolism as a response to thermal trauma only can be modulated, not completely reversed. The burn wound consumes large quantities of energy during the healing process due to the large population of inflammatory cells and the production of collagen and matrix by fibroblasts. Postburn, the metabolic and catabolic responses are prolonged in severity and time course, lasting weeks to months in contrast to the days and weeks observed in other injuries.

Therapeutic strategies should aim to prevent body weight losses of more than 10% of patients baseline status because more profound weight losses are associated with significantly worse outcomes [1]. Known consequences of catabolic disorders with loss of lean body mass above 10% include impaired immune function and delayed wound healing. Lean body mass reduction beyond 40% leads to imminent mortality.

Therefore, complications of ongoing catabolism remain a major cause of morbidity and mortality in severely burned patients. In addition to optimizing nutrient intake, anticatabolic and anabolic agents that may counteract “the stress response to injury or illness” may be of significant clinical benefit [2].

1.1. Enteral versus parenteral nutrition

There is overwhelming evidence that the enteral route for nutrition delivery is far superior to the parenteral route [3]. The reasons are clear and multifactorial.

Total parenteral nutrition (TPN) has been shown to be ineffective in preventing the catabolic response after burn injury. Total parenteral nutrition enhances the stress response, increases endotoxin translocation [4] and leads to an impairment of mucosal immunity [5]. Total parenteral nutrition has been shown to increase the expression of TNF-α mRNA in

* Corresponding author. Tel.: +43-1-40400-6860; fax: +43-1-40400-6862.
E-mail address: harald.andel@univie.ac.at (H. Andel).

0305-4179/$30.00
doi:10.1016/S0305-4179(03)00069-X

organ tissues with increase in systemic TNF-α production, and to lead to a reduction in survival rate after thermal injury [6].

Immediate postburn total enteral nutrition can provide better nutritional support than total parenteral nutrition through the maintenance of gut mucosal integrity and the prevention of increased secretion of catabolic hormones. Total enteral nutrition provides better regulation of inflammatory cytokine responses and may contribute less to immunosuppression after major surgery than parenteral nutrition [7]. Furthermore, total enteral nutrition may decrease intestinal permeability, preserve the intestinal mucosal barrier and have a beneficial effect on the reduction of enterogenic infection [8].

Contrary to the usual clinical practice of supplemental parenteral nutrition during the first postburn days, immediate high calorie enteral feeding during the postburn shock phase has a positive effect on splanchnic perfusion [9].

Although, supplemental parenteral nutrition enhances nutrient intake and corrects nutritional parameters such as retinol-binding protein and prealbumin more rapidly, it has no clinically relevant effect on outcome in ICU patients at the early phase of nutritional support [10]. More notably, in burned patients supplemental parenteral nutrition leads to a significant increase in mortality [38].

1.2. Gastric versus duodenal feeding

There is a presumed increase in the risk of ventilator-associated pneumonia with tube feeding. This has stimulated the development of procedures for duodenal intubation and feeding as primary prophylaxis to prevent ventilator-associated pneumonia. Currently, no clear difference in the incidence of ventilator-associated pneumonia in duodenal compared with gastric enteral nutrition can be shown [11].

However, gastric feeding in the first postburn day is known to have a 18% failure rate due to regurgitation [3]. Furthermore, using the duodenal approach even early high-calorie feeding is very well tolerated with nearly 100% success rate [9]. Therefore, duodenal feeding seems to be superior to gastric feeding at least in the immediate feeding regime after admission.

1.3. Overfeeding

Although an enteral high-carbohydrate diet improves the net balance of skeletal muscle protein [12], in surviving burned patients, calorie delivery beyond 1.2 × resting energy expenditure results in increased fat mass without changes in lean body mass [13]. Moreover, high-carbohydrate diet often leads to hyperglycemia, which has been shown to be of negative influence on the outcome of septic and critically ill patients [14,15]. Furthermore, high calorie enteral nutrition may lead to an impairment of the splanchnic oxygen balance in burned septic patients [16].

The use of the formulae of Harris and Benedict or Curreri for prediction of resting energy expenditure has not been validated in patients with more than 40% body surface area burned. Therefore, in order to prevent a negative impact on the outcome of these patients measurement of resting energy expenditure and gastric CO_2-gap, as a parameter for splanchnic oxygen balance, is recommended.

Resting energy expenditure seems to be very variable in those patients and declining energy expenditure appears to be a harbinger of mortality in severely burned patients [13].

1.4. Specific formulae of enteral nutrition for specific metabolic abnormalities

Burn injury results in profound metabolic abnormalities, whereas the range of metabolic demands varies with the severity of the burn injury. The increase in endogenous catabolic hormones, primarily cortisol, and catecholamines and a decrease in the normal endogenuous activity of the anabolic agents combine to result in a large protein loss [17]. Therefore, and especially for wound healing, protein rich nutrition formulas should be used.

The impact of special substrates on the progress of burn disease is still under discussion. However, there is growing evidence that agents such as glutamine, have positive impact on metabolic management and thereby on morbidity and outcome in severely burned patients [18–21]. On the other hand the overall effect of glutamine in humans is still under discussion, because limited data are available concerning the mechanism for any of the glutamines purported effects. Moreover, whether these effects are based on altered cellular physiology, metabolic regulation, or regulation of gene expression is still unclear [22].

Arginine has been shown to have a wide variety of potentially beneficial metabolic effects, since it serves multiple roles in the pathophysiological response in injured and critical patients. The rate of arginine degradation is markedly increased after burn, whereas synthesis remains constant, leading to a deficiency state [23].

Nutritional intervention using omega-3 fatty acid leads a more rapid recovery of serum insulin like growth factor (IGF) levels with consecutive beneficial effects on wound healing [24].

1.5. Role of anabolic and anticatabolic agents

An additional major problem for the burn patient is the fact that, despite an inevitable lean body mass—loss of 10% or more over a several week period, the rate of restoration of lost body protein is about 1/10 as rapid even with adequate nutrition and exercise. The reason is that the endogenuous stimulus returns to normal during recovery but does not exceed normal yet all the cells are primed for anabolism and respond to any added anabolic stimulus with increased protein synthesis [17]. Several hormones have been shown to

be efficient in increasing protein synthesis during the acute and recovery phases of burn injuries.

In spite of the fact that agents such as human growth hormon (hGH), the testosterone derivative oxandrolone and IGF reduce catabolism and muscle mass reduction [25–30], the impact of hGH on the course of disease and its outcome is still controversial [31–33].

Further on, low-dose insulin has anabolic effects [31] and might have a beneficial effect on the outcome. Hyperglycemia or relative insulin deficiency, or both during critical illness may confer a predisposition to complications, such as severe infections, multiple organ failure and death [15]. High calorie fed critically ill burned patients are at special risk for development of high blood sugar levels. Elevations in plasma glucose concentration impair immune function by altering cytokine production from macrophages, diminishing lymphocyte proliferation and depressing intracellular bactericidal activity of leucocytes [34]. However, is still not known whether the blood sugar level or insulin by itself is responsible for the better outcome [14]. In burned patients beneficial effects can be expected by a combination of increased immune response due to lower blood sugar levels and improved wound healing due to insulin by itself.

A completely different approach in the treatment of catabolism is the use of β-blocking agents in severe burned patients. At least in burned children administration of propanolol attenuates hypermetabolism and reverses muscle–protein catabolism without side effects on wound healing [35]. Ensuring adequate tissue perfusion is of utmost importance for the wound healing and the outcome of burned patients. β-Blockade diminishes peripheral perfusion and might lead thereby to a conversion of intermediate thickness to full thickness wounds. Herndon et al. [35] did not see this effect due to β-blockade in children, adult patients might respond differently because of a different structure of the skin. Furthermore, the better wound healing capacity in children [36] might have prevented potential negative effects of β-blockade associated with diminished perfusion.

Beside this, β-blockade of septic patients is contrary to the hyperperfusion-concept of Shoemaker et al [37]. Although this concept has been widely discussed, regional hypoperfusion, even without β-blockade, is a known problem in septic burned patients [16].

The overall effect of β-blockade on the outcome of severely burned children and adults is still not known, as less catabolism does not necessarily result in a better survival rate.

2. Practical recommendations

Based on the literature, total enteral nutrition is the preferable feeding method for severely burned patients. Total enteral nutrition should start as early as possible without any supplemental parenteral nutrition and can be increased very rapidly. Using a duodenal approach, especially in the early postburn phase, seems to be superior to gastric feeding as patients given feeding into the small intestine do tolerate higher calorie and protein intakes.

The clinical routine of slowly increasing the amount of enteral nutrition in the early postburn phase with supplemental parenteral nutrition is inferior to an early high calorie total enteral nutrition approach. However, administration of high calorie total enteral nutrition in a later septic phase should be critically reviewed due to possible impairment of splanchnic oxygen balance. Therefore, measurement of the CO_2-gap seems to be a useful tool in determining nutrition dependent oxygen imbalances of the intestine in critical ill patients and should be considered as a monitoring method during small bowel nutrition.

The use of supplements such as arginine, glutamine and vitamins is a promising field for future studies but the real impact on the course of disease and its outcome is not yet decided.

Similarly, reviewing the literature provides contradictory data on the impact of the use of anabolic and anticatabolic agents. Recently published data on β-blockade offer new aspects on the metabolic management of burned patients. Whereas, in children β-blockade seems to be of clear benefit on catabolism, in adults similar data is not yet available. In particular the impact of β-blockade on the outcome of severely burned patients remains to be evaluated as does.

The effect of insulin administration and low blood sugar regimes on wound healing and outcome in burned patients.

3. Conclusion

In the recent literature discussion on the advantages of enteral versus parenteral nutrition and on gastric versus duodenal feeding can still be found. Furthermore, high calorie nutrition and the possibility of overfeeding are important aspects in burned patients. Specific formulas of enteral nutrition for specific metabolic abnormalities are currently under evaluation as are the roles of anabolic and anticatabolic agents.

References

[1] Chang DW, DeSanti L, Demling RH. Anticatabolic and anabolic strategies in critical illness: a review of current treatment modalities. Shock 1998;10(3):155–60.
[2] Demling RH, DeSanti L. Involuntary weight loss and the nonhealing wound: the role of anabolic agents. Adv Wound Care 1999;12(1 Suppl):1–14.
[3] McDonald WS, Sharp Jr CW, Deitch EA. Immediate enteral feeding in burn patients is safe and effective. Ann Surg 1991;213(2):177–83.
[4] Sugiura T, Tashiro T, Yamamori H, Takagi K, Hayashi N, Itabashi T, et al. Effects of total parenteral nutrition on endotoxin translocation and extent of the stress response in burned rats. Nutrition 1999;15(7-8):570–5.
[5] Renegar KB, Kudsk KA, Dewitt RC, Wu Y, King BK. Impairment of mucosal immunity by parenteral nutrition: depressed nasotracheal

influenza-specific secretory IgA levels and transport in parenterally fed mice. Ann Surg 2001;233(1):134–8.
[6] Cui XL, Iwasa M, Kuge H, Sasaguri S, Ogoshi S. Route of feeding influences the production and expression of tumor necrosis factor alpha in burned rats. Surg Today 2001;31(7):615–25.
[7] Takagi K, Yamamori H, Toyoda Y, Nakajima N, Tashiro T. Modulating effects of the feeding route on stress response and endotoxin translocation in severely stressed patients receiving thoracic esophagectomy. Nutrition 2000;16(5):355–60.
[8] Peng YZ, Yuan ZQ, Xiao GX. Effects of early enteral feeding on the prevention of enterogenic infection in severely burned patients. Burns 2001;27(2):145–9.
[9] Andel H, Rab M, Andel D, Felfernig M, Horauf K, Felfernig D, et al. Impact of early high caloric duodenal feeding on the oxygen balance of the splanchnic region after severe burn injury. Burns 2001;27(4):389–93.
[10] Bauer P, Charpentier C, Bouchet C, Nace L, Raffy F, Gaconnet N. Parenteral with enteral nutrition in the critically ill. Intensive Care Med 2000;26(7):893–900.
[11] Kearns PJ, Chin D, Mueller L, Wallace K, Jensen WA, Kirsch CM. The incidence of ventilator-associated pneumonia and success in nutrient delivery with gastric versus small intestinal feeding: a randomized clinical trial. Crit Care Med 2000;28(6):1742–6.
[12] Hart DW, Wolf SE, Zhang XJ, Chinkes DL, Buffalo MC, Matin SI, et al. Efficacy of a high-carbohydrate diet in catabolic illness. Crit Care Med 2001;29(7):1318–24.
[13] Hart DW, Wolf SE, Herndon DN, Chinkes DL, Lal SO, Obeng MK, et al. Energy expenditure and caloric balance after burn: increased feeding leads to fat rather than lean mass accretion. Ann Surg 2002;235(1):152–61.
[14] Gore DC, Chinkes D, Heggers J, Herndon DN, Wolf SE, Desai M. Association of hyperglycemia with increased mortality after severe burn injury. J Trauma 2001;51(3):540–4.
[15] Van Den Berghe G, Wouters P, Weekers F, Verwaest C, Bruynïnckx F. Intensive insulin therapy in critically ill patients. N Engl J Med 2001345(19):1359–67.
[16] Andel H, Rab M, Andel D, Hörauf K, Felfernig D, Schramm W, et al. Impact of duodenal feeding on the oxygen balance of the splanchnic region during different phases of severe burn injury. Burns 2002;28(1):60–4.
[17] Demling RH, Seigne P. Metabolic management of patients with severe burns. World J Surg 2000;24(6):673–80.
[18] Jeschke MG, Herndon DN, Ebener C, Barrow RE, Jauch KW. Nutritional intervention high in vitamins, protein, amino acids, and omega 3 fatty acids improves protein metabolism during the hypermetabolic state after thermal injury. Arch Surg 2001;136(11): 1301–6.
[19] Wilmore DW. The effect of glutamine supplementation in patients following elective surgery and accidental injury. J Nutr 2001;131(9 Suppl):2543S–9S, discussion 2550S-1S.
[20] Gore DC, Jahoor F. Deficiency in peripheral glutamine production in pediatric patients with burns. J Burn Care Rehabil 2000;21(2):171, discussion 172-7.
[21] Houdijk AP, Rijnsburger ER, Jansen J, Wesdorp RI, Weiss JK, McCamish MA, et al. Randomised trial of glutamine-enriched enteral nutrition on infectious morbidity in patients with multiple trauma. Lancet 1998;352(9130):772–6.
[22] Buchman AL. Glutamine: commercially essential or conditionally essential? A critical appraisal of the human data. Am J Clin Nutr 2001;74(1):25–32.
[23] Yu YM, Ryan CM, Castillo L, Lu XM, Beaumier L, Tompkins RG, et al. Arginine and ornithine kinetics in severely burned patients: increased rate of arginine disposal. Am J Physiol Endocrinol Metab 2001;280(3):E509–17.
[24] Abribat T, Nedelec B, Jobin N, Garrel DR. Decreased serum insulin-like growth factor-I in burn patients: relationship with serum insulin-like growth factor binding protein-3 proteolysis and the influence of lipid composition in nutritional support. Crit Care Med 2000;28(7):2366–72.
[25] Hart DW, Herndon DN, Klein G, Lee SB, Celis M, Mohan S, et al. Attenuation of posttraumatic muscle catabolism and osteopenia by long-term growth hormone therapy. Ann Surg 2001;233(6):827–34.
[26] Hart DW, Wolf SE, Ramzy PI, Chinkes DL, Beauford RB, Ferrando AA, et al. Anabolic effects of oxandrolone after severe burn. Ann Surg 2001;233(4):556–64.
[27] Ferrando AA, Sheffield-Moore M, Wolf SE, Herndon DN, Wolfe RR. Testosterone administration in severe burns ameliorates muscle catabolism. Crit Care Med 2001;29(10):1936–42.
[28] Demling RH, DeSanti L. The rate of restoration of body weight after burn injury, using the anabolic agent oxandrolone, is not age dependent. Burns 2001;27(1):46–51.
[29] Akcay MN, Akcay G, Solak S, Balik AA, Aylu B. The effect of growth hormone on 24-h urinary creatinine levels in burned patients. Burns 2001;27(1):42–5.
[30] Demling RH, Orgill DP. The anticatabolic and wound healing effects of the testosterone analog oxandrolone after severe burn injury. J Crit Care 2000;15(1):12–7.
[31] Zhang XJ, Chinkes DL, Wolf SE, Wolfe RR. Insulin but not growth hormone stimulates protein anabolism in skin wound and muscle. Am J Physiol 1999;276(4 Pt 1):E712–20.
[32] Takala J, Ruokonen E, Webster NR, Nielsen MS, Zandstra DF, Vundelinckx G, et al. Increased mortality associated with growth hormone treatment in critically ill adults. N Engl J Med 1999; 341(11):785–92.
[33] Demling RH. Comparison of the anabolic effects and complications of human growth hormone and the testosterone analog, oxandrolone, after severe burn injury. Burns 1999;25(3):215–21.
[34] Reinhold D, Ansorge S, Schleicher ED. Elevated glucose levels stimulate transforming growth factor-beta 1 (TGF-beta 1), suppress interleukin IL-2, IL-6 and IL-10 production and DNA synthesis in peripheral blood mononuclear cells. Horm Metab Res 1996;28(6):267–70.
[35] Herndon DN, Hart DW, Wolf SE, Chinkes DL, Wolfe RR. Reversal of catabolism by beta-blockade after severe burns. N Engl J Med 2001;345(17):1223–9.
[36] Swift ME, Burns AL, Gray KL, DiPietro LA. Age-related alterations in the inflammatory response to dermal injury. J Invest Dermatol 2001;117(5):1027–35.
[37] Shoemaker WC, Appel PL, Kram HB, Bishop M, Abraham E. Hemodynamic and oxygen transport monitoring to titrate therapy in septic shock. New Horiz 1993.
[38] Herndon DN, Barrow RE, Stein M, Linares H, Rutan TC, Rutan R, et al. Increased mortality with intravenous supplemental feeding in severely burned patients. J Burn Care Rehabil 1989;10(4):309–13.